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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
07/23/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/595,709	GRASES FREIXEDAS, FELICIA	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response, filed 04/01/09, has been fully considered and made of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is made final.

Status of the Claims

Claims 8-19 are currently pending in this application and are the subject of the Office action.

Miscellaneous

It is suggested that claims 8 and 14 be amended to further clarify the claimed subject matter by deleting the term "where the calcification is generated" and replacing it with the term "where the calcification is generated in said soft tissue."

REJECTION

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the

subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-19 are rejected under 103(a) as being unpatentable over Kamiya et al. (US Patent Application Pub. No. 2003/0119910), in view of Bissett et al. (US Patent 5,821,237), as evidenced by Horrobin et al. (Us patent 5,516,801).

Kamiya et al. teach methods of treating or preventing aging-associated diseases caused by a decrease in the expression of Klotho protein in animals or humans, including aging, ectopic calcification, skin involution, arteriosclerosis, hyperlipidemia, hypertension, cerebral apoplexy, diabetes, senile dementia of Alzheimer type (paras. 0022-0023). In particular, Kamiya et al. teach compositions comprising phosphorus

containing compounds, such as phytic acid, for treating said diseases in animals or humans (abstract; para. 0081). Also, Kamiya et al. disclose that it is desirable to administer said compositions by any desirable route that is most effective for the treatment, including non-oral routes (para. 0044).

Although Kamiya et al. teach methods of treating aging associated diseases (e.g. **ectopic calcification**) in an animal or human comprising administering a composition containing phytic acid by non-oral routes, this reference does not specifically teach the instantly claimed method step of topically applying the myo-inositol hexaphosphate (= phytic acid) composition to treat/prevent pathological calcifications.

Bissett et al. teach methods of treatment for improving the visual appearance of skin comprising administering topical compositions comprising myoinositol compounds, wherein said topical compositions are in the forms such as lotions, creams and ointments (abstract, and col. 6, line 35 to col. 8, line 52; col. 13, lines 29-59). Bissett et al. teach that methods comprising **topically applying to the skin an effective amount of the compositions in a subject so as to deposit an effective amount of the primary actives (e.g. myoinositol compound such as myo-inositol hexakisphate dodecasodium salt and phytic acid) on the skin**, wherein the primary actives are left in contact with the skin for a period of at least several hours e.g. about 4 to about 12 hours); the compositions may be applied from about three times a day to about once every other day (col. 23, line 66 to col. 24, line 38; see also col. 4, line 43 to col. 8, line 51). In particular, Bissett et al. exemplify compositions comprising phytic acid in a **concentration range of 1 to 5 %** (cols. 25, line 40 to col. 27, line 49). Also, Bissett et

al. disclose a regimen for applying said compositions to the skin one time per week at a level of 5 mg/cm2 over a three-year period to regulate skin wrinkles.

Horrobin et al. is added only as an evidentiary reference to show that ectopic calcifications involve various soft tissues, including blood vessels, kidney, skin, and brain (col. 2, lines 14-32).

It would have been obvious to a person of skill in the art at the time the invention was made to combine the cited references by modifying the route of administration of the composition as taught by Kamiya et al. by applying said composition topically to skin as taught by Bissett et al. to treat or prevent a pathological calcification in a soft tissue (e.g. ectopic calcification) as taught by Kamiya et al. in order to improve/prevent the symptoms caused by calcification. One would have been motivated to do so because Kamiya et al. suggest that compositions comprising phytic acid can be administered by any desirable route, including non-oral routes such as subcutaneous methods, and the method of topically applying phytic acid compositions to the skin as taught by Bissett et al. is also a non-oral route. Further, one would reasonably expect that the topical administration/application to the skin of a composition comprising the identical instantly claimed myo-inositol hexaphosphate (phytic acid) as taught by the Kamiya et al. and Bissett et al. would be absorbed by the skin and then travel via the bloodstream to the target site where the calcification is generated, including the subepithelial tissue, renal tissue, pulmonary tissue, cerebral tissue, and the wall of a blood vessel because both Kamiya et al. and Bissett et al. teach therapeutically effective compositions and it is well known that drugs that are applied to the skin do get absorbed by the skin and then get

distributed throughout the body via the bloodstream. Besides, both Kamiya et al. and Bissett et al. teach compositions for treating aging-associated conditions (e.g. skin wrinkles), which overlaps with the instant claimed population (i.e. ectopic calcification) as evidenced by the teaching of Kamiya et al. and Horrobin et al. such that one would expect that administration of the same drug (phytic acid) as taught by the prior art to the same instantly claimed population (ectopic calcification) would also have the same therapeutic effects absence evidence to the contrary.

It is noted that the instant application discloses that ectopic calcifications are common alterations associated with soft tissues, mainly skin, kidney, tendons, and cardiovascular tissues (page 1, lines 16-18).

It is also noted that applicant exemplifies compositions comprising sodium phytate 2.9% (2% phytate), sodium phytate 0.7% (0.5% phytate), sodium phytate 2.5% (1.7% phytate), which overlap with the above referenced teaching of Bissett et al. of concentrations of phytic acid in the range of from 1-5% of phytic acid (see specification, pages 7-9).

With respect to the preamble of claim 14, it is noted that Kamiya et al. teach methods for preventing aging-associated diseases, including ectopic calcification, comprising administering compositions comprising phytic acid (para. 0081).

With respect to the limitations recited in dependent claims 9-13 and 15-19, it is noted that Kamiya et al. teach aging-associated diseases including ectopic calcification, which overlaps with the instant claimed population (pathological calcification in a soft tissue). Since ectopic calcification involves soft tissues, including skin, brain, kidney, and blood

vessels, one would reasonably expect that the method of treatment comprising topically administering the same instantly claimed compound as taught by the prior art would also be effective in treating/ preventing pathological calcification involving subepithelial tissue, renal tissue, pulmonary tissue, cerebral tissue, and the wall of a blood vessel as evidenced by the teaching of Horrobin et al. (col. 2, lines 14-32).

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Response to applicant's arguments/remarks

In response to applicant's assertion that one would not reasonably expect to select ectopic calcification from the laundry list of possible diseases prevented or treated under the heading "disease caused by a decrease in the expression of Klotho protein as taught by Kamiya et al. for treatment with compositions comprising a phosphorous containing compound (e.g. phytic acid), it is noted that Kamiya et al. provides a general teaching of diseases associated with a decrease in the expression of Klotho protein in animals or humans (e.g. aging, ectopic calcification, skin involution, osteoporosis, alopecia; paras. 0022-0026) such that one would reasonably expect that the genus of diseases associated with a decrease in the expression of Klotho protein in animals or humans would be representative of the various species encompassed by said genus since each disease/condition species of the genus is associated with a decreased level Klotho protein. Besides, applicant has not provided any objective evidence to show that the method of treatment encompassed by the prior art does not

work for treating ectopic calcifications or skin aging conditions. Further, Kamiya et al. teach methods of treating diseases/conditions associated with Klotho protein, wherein said conditions/diseases may be preferably prevented/treated with compositions comprising ornithine and at least one compound selected from the group consisting of compounds containing a divalent cationic metal and compounds containing phosphorus (e.g. phytic acid = phosphorus containing compound; para. 0078-0081) and Bissett et al. teach methods of treating skin wrinkles (= condition associated with aging skin; col. 1, lines 17-67) comprising topical depositing (= applying) on the skin of a subject a composition comprising a skin repair active agent (e.g. phytic acid = phosphorus containing compound; col. 3, line 2 to col. 8, line 51; and cols. 25-26, Examples 2-7). Hence, applicant's argument that one would not reasonably expect to extrapolate the teaching of Kamiya et al. to the genus of conditions/diseases associated with a decrease in Klotho protein is not found to be persuasive because ectopic calcification is associated the skin as evidenced by the teaching of Horrobin et al. that ectopic calcifications involve various soft tissues, including skin (col. 2, lines 14-32) and skin wrinkles as taught by Bissett et al. is a condition associated with aging. Since ectopic calcification as taught by Kamiya et al. involves the skin, which is a soft tissue, and the instant claims are directed to a method of treating a pathological calcification in a soft tissue (= ectopic calcification of the skin), one would reasonably expect that topical application of a composition encompassed by the prior art comprising a safe and effective amount of a phosphorus containing compound (e.g. phytic acid) as taught by Bissett et al. to a patient with an ectopic calcification of the skin as taught by Kamiya et

al. would have the same pharmacokinetic/therapeutic effect as claimed, including resulting the absorption of said composition by the skin, followed by distribution via the bloodstream and exerting a therapeutic effect at the site of ectopic calcification (= acting where the calcification is generated).

In response to applicant's argument that Kamiya et al. disclose compounds containing phosphorus that is intended to facilitate the administration in the feed or food and drink (para. 78) and that ornithine is the agent responsible for the therapeutic effect in treating diseases caused by a decrease in the expression of Klotho (para. 40 and 43), it is noted that Kamiya et al. disclose methods of treating/preventing diseases/conditions associated with Klotho protein that may be preferably prevented/treated with compositions comprising ornithine and at least one compound selected from the group consisting of compounds containing a divalent cationic metal and **compounds containing phosphorus** (e.g. phytic acid; para. 0078-0081) and Bissett et al. teach topical compositions comprising phytic acid as the primary skin active agent (cols. 25-26, Examples 2-7). Since the instant claims 8 and 14 recite the transitional phrase "comprising," one would reasonably envisage the inclusion of other agents in the ornithine containing composition of Kamiya et al. (e.g. phytic acid; para. 0081) for treating a human with diseases/conditions associated with Klotho protein (e.g. ectopic calcification of the skin). Hence, applicant's arguments regarding the lack of disclosure of the biological effect of the phosphorus compounds of Kamiya et al. is not found to be persuasive.

In response to applicant's argument that one of skill in the art would not consider phytic acid as a substitute for inorganic phosphorus salts (CaHPO4 and KH2PO4) since only inorganic salts (CaHPO4 and KH2PO4) are disclosed, it is noted that it is routine in the art to employ the salts forms of known compounds depending on the specific components and carrier used in the composition and applicant has not provided any objective evidence to show phytic acid does not work when it is applied topically to the skin.

In response to applicant's assertion that one would not combine the teachings of Kamiya and Bissett because topical application of the composition comprising myo-inositol as taught by Bissett et al. is intended to exhibit a cosmetic effect and would not be expected to reach the blood stream (or to have a systemic effect), it is noted that Kamiya et al. teach that ectopic calcifications and aging are associated with a decrease in Klotho protein (para. 0002) and Bissett et al. teach a method for regulating skin wrinkles (= skin aging condition; col. 1, lines 24-27) comprising topically applying a safe and effective amount of a composition comprising myo-inositol to the skin (cols. 25-26; see also col. 3, lines 17-31). It is also noted that applicant exemplifies compositions comprising sodium phytate 2.9% (2% phytate), sodium phytate 0.7% (0.5% phytate), sodium phytate 2.5% (1.7% phytate), which overlap with teaching of Bissett et al. of concentrations of phytic acid in the range of from 1-5% of phytic acid (see specification, pages 7-9). Hence, one would reasonably expect that topical application of myo-inositol in an effective amount to regulate skin wrinkles as taught by Bissett et al. would also be effective to treat diseases/conditions associated with a decreased level of Klotho protein

(e.g. ectopic calcification and aging) since Kamiya et al. teach that aging is associated with a decreased level of Klotho protein and skin wrinkles as taught by Bissett et al. is also associated with aging. Hence, it is the examiner's position that one would reasonably expect to rely on the teaching of Kamiya et al. in view of Bissett et al. since both references are concerned with methods of treating the aging skin comprising employing compositions comprising phosphorus containing drugs (i.e. phytic acid). Since the prior art teaches every claim limitation, one would reasonably expect that topical application of a composition comprising the identical instantly claimed myoinositol in an effective amount to treat skin wrinkles as taught by Bissett et al. would also be effective to treat pathological calcification in a soft tissue as claimed since Kamiya et al. suggest that methods of treatment comprising administering compositions comprising a phosphorus containing compound and ornithine are useful for treating conditions associated with a decreased level of Klotho protein and both ectopic calcification and skin aging/skin wrinkles are believed to be associated with a decreased level of Klotho protein as evidenced by the teaching of Kamiya et al. (paras 0002-0003). Hence, applicant's argument that Bissett's invention is focused on the outer part of the skin, while the instant application is focused the skin serves as an entrance way in order to eventually reach the blood stream is not found to be sufficient to patentably distinguish the instant claimed invention from the prior art.

Relevant Art of Record

The below cited art made of record and relied upon is considered pertinent to applicant's invention.

Galvin et al. (US Patent 6,359,194) teach methods for screening compounds and other substances for treating cardiovascular disease symptoms, including cardiac calcification, hemorrhagic telangiectasia, advanced atherosclerosis and/or plaque rupture, cardiovascular calcification (col. 8, line 64 to col. 9, line 22).

Hippocrates et al. report that five patients on maintenance hemodialysis for more than five years, who had tumoral calcifications, were treated by sodium thiosulfate. Four patients with periarticular and soft-tissue calcifications achieved regression of varying degrees and the motion of the adjacent joints was considerably improved (Hippocrates et al. Sodium thiosulfate treatement of soft-tissue calcifications in patients with end-stage renal disease. Perit Dial Int. 1987;7(4):250-252, abstract only). The fifth patient had calcification of penis; sodium thiosulfate produced early relief of symptoms and later complete disappearance of the calcification.

Steidl et al. teach a method of treating patients suffering from myositis ossifications traumatica comprising local application of magnesium sulfate under local anesthesia into calcified areas for 2-20 weeks (Steidl et al. Soft tissue calcification treated with local and oral magnesium therapy. Magnes Res. 1990;3(2):113-9, abstract only). Steidl et al. teach that said treatment resulted in the disappearance or substantial reduction of the soft tissue calcifications (abstract).

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov.

Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

9 July 2009

/C. R./ Examiner, Art Unit 1611

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